(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 July 2001 (19.07.2001)

PCT

(10) International Publication Number
WO 01/51909 A1

(51) International Patent Classification[7]: G01N 1/31

(21) International Application Number: PCT/US01/00512

(22) International Filing Date: 8 January 2001 (08.01.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/483,248 14 January 2000 (14.01.2000) US

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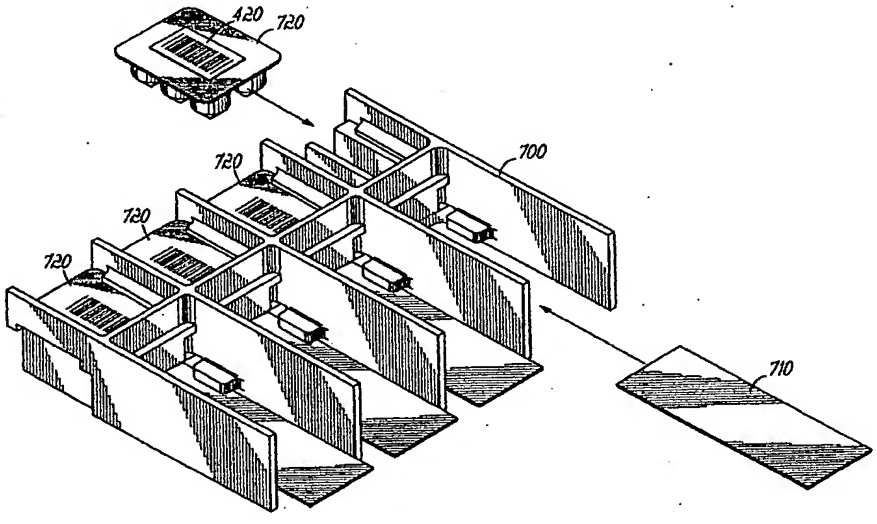
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD AND APPARATUS FOR AUTOMATIC TISSUE STAINING



(57) Abstract: A method and apparatus for specimen slide (710) preparation is disclosed. The method and apparatus of the present invention uses slide trays (700) that have receptacles for at least one specimen slide (710) and an associated reagent park (720). The specimen slide (710) and/or reagent pack (720) includes an identifier (420) that specifies a particular slide preparation protocol that should be followed. The method and apparatus reads the identifier (420) to determine the particular slide preparation protocol and then prepares the specimen slide according to the particular slide preparation protocol. The apparatus may obtain some or all of the reagents needed for the particular slide preparation protocol from the reagent pack (400).

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METHOD AND APPARATUS FOR AUTOMATIC TISSUE STAINING

Field of the Invention

The present invention relates to the field of medical lab equipment. In particular the present invention discloses a fully automated system for staining tissue specimens and cell preparations.

Background of the Invention

A normal function of medical laboratories is to examine cells and cell tissue under a microscope. The lack of contrast between individual cells and the background matrix or between individual parts of cells can make it difficult to examine cell and tissue preparations. To improve the contrast, researchers have applied stains to cell and tissue specimens to be examined. The stains are absorbed differently by the various structures in cells such that the contrast between the different cell structures is improved.

Staining tissue specimens is a nontrivial time consuming process. Often a number of different staining and rinsing stages are required. Each stage requires a specific amount of reagent or buffer and

takes a specific amount of time. Thus, trained technicians are often employed to perform such operations. Furthermore, hospitals and laboratories must stain very large numbers of tissue specimens for patient diagnoses. Thus, automated tissue staining systems have been developed. By automating the process, expensive human labor is eliminated. Furthermore, automatically staining specimens significantly reduces the probability of an error occurring during the staining process.

To ensure that the proper staining procedures are followed, most automatic staining systems require that the user carefully enter the staining protocol and load the proper reagents. The complicated procedures require user training before such devices can be operated effectively. It would therefore be desirable to simplify the operation of an automatic tissue-staining device.

Summary of the Invention

A method and apparatus for specimen slide preparation is disclosed. The method and apparatus of the present invention uses slide trays that have receptacles for at least one specimen slide and an associated reagent pack. The specimen slide and/or reagent pack includes an identifier that specifies a particular slide preparation protocol that should be followed. The method and apparatus reads the identifier to determine the particular slide preparation protocol and then prepares the specimen slide according to the particular slide preparation protocol. The apparatus may obtain some or all of the reagents needed for the particular slide preparation protocol from the reagent pack.

Other objects feature and advantages of present invention will be apparent from the drawings and the detailed description that follows.

Brief Description of the Drawings

The objects, features, and advantages of the present invention will be apparent to one skilled in the art, in view of the following detailed description in which:

Figure 1A illustrates a cut-away view of a first tiltable sink assembly embodiment.

Figure 1B illustrates the tiltable sink assembly of Figure 1A wherein the tiltable sink assembly is tilted to the right.

Figure 1C illustrates the tiltable sink assembly of Figure 1A wherein the tiltable sink assembly is tilted to the left.

Figure 2A illustrates a cut-away view of a second tiltable sink assembly embodiment.

Figure 2B illustrates the tiltable sink assembly of Figure 2A wherein the tiltable sink assembly is tilted to the right.

Figure 2C illustrates the tiltable sink assembly of Figure 2A wherein the tiltable sink assembly is tilted to the left.

Figure 3 illustrates a conceptual diagram of the internal fluid flow components of the autostainer apparatus.

Figure 4a illustrates a first arrangement of a reagent pack for the autostainer apparatus of the present invention.

Figure 4b illustrates a second arrangement of a reagent pack for the autostainer apparatus of the present invention.

Figure 5a illustrates a four well reagent pack or the autostainer apparatus of the present invention.

Figure 5a illustrates a six well reagent pack or the autostainer apparatus of the present invention.

Figure 5c illustrates an eight well reagent pack or the autostainer apparatus of the present invention.

Figure 6a illustrates a first embodiment of bulk packaged reagent packs.

Figure 6b illustrates a second embodiment of bulk packaged reagent packs.

Figure 7a illustrates a front view of a combined slide and reagent rack for preparing four slides.

Figure 7b illustrates a back view of a combined slide and reagent rack for preparing four slides.

Figure 8A illustrates a flow diagram of the general operation of the autostainer apparatus.

Figure 8B illustrates a flow diagram summary of the slide protocol scheduling system of the autostainer control program.

Figure 9a through 9d illustrate a flow diagram describing the details of adding a new slide to the Currently Scheduled Array (CSA).

Detailed Description of the Preferred Embodiment

A method and apparatus for automatically staining tissue specimens is disclosed. In the following description, for purposes of explanation, specific nomenclature is set forth to provide a thorough

understanding of the present invention. However, it will be apparent to one skilled in the art that these specific details are not required in order to practice the present invention. For example, the present invention has been described with reference to staining of tissue specimens. However, the same techniques can easily be applied to other types of slide preparation work.

The Autostainer Hardware

The present invention comprises advances in automated slide staining. An example of an automatic slide staining apparatus can be found the first figure of U.S. Patent 5,839,091, issued November 17, 1998, and entitled "Method and apparatus for automatic tissue staining" which is hereby incorporated by reference in its entirety. An autostainer system is used for staining tissue specimens that are placed onto glass slides. The present invention uses several different slide racks wherein each slide rack holds one or more slides. In one embodiment, there are six slide racks and each slide rack is capable of holding four slides such that the autostainer can prepare twenty-four different slides simultaneously.

An autostainer uses a robotic delivery system that delivers bulk reagents, small supply reagents, buffer solutions, and air to the glass slides. The robotic delivery system is controlled by a computer system. The computer system executes an autostainer control program that sends control commands to control the robotic delivery system. In one embodiment, the robotic delivery system of the autostainer consists of an X-axis mechanism, a Y-axis mechanism, and a Z head as illustrated in U.S.

Patent 5,839,091. The Z head has a Bulk fluid dispensing tube for dispensing a few selected bulk reagents and buffer rinse solution, an air blade to blow air onto slides, and a syringe probe for picking up reagents that will be placed onto the glass slides.

To prevent contamination, the syringe probe is cleaned in a reagent probe wash bin between the uses of different reagents. The wash bin has three different receptacles that are used in three stages. The first hole is used to rinse the inside of the probe by forcing buffer rinse solution through the inside of probe and down into a first drain receptacle. The second receptacle is used to clean the outside of the probe by forcing buffer rinse solution through the inside of probe while the probe is in the tightly confined second receptacle such that the buffer solution is force upward on the outside of the probe. Finally, the probe is placed into a third receptacle and air is forced through the probe to clean out the buffer rinse solution.

Beneath the slide racks of the autostainer is a sink assembly. The sink assembly catches the reagents and buffer rinse solution that drip off the slides. Figure 1A illustrates a cut-away top view of a first embodiment of a sink assembly. As illustrated in Figure 1A, a tiltable sink 210 sits beneath a support bracket 205 for the slide racks (not shown). The tiltable sink 210 may be tilted left or right using a tilt mechanism 220. When the tiltable sink 210 is tilted down on the right side as illustrate in Figure 1B, all the liquid waste spilling off the slides will drain out of drain hole 231 on the right side, through corrugated tubing 241 and drain pipe 251, and finally to a waste line #1 (not shown). Similarly, when the tiltable

sink 210 is tilted down on the left side as illustrated in Figure 1C, all the liquid waste will drain out of drain hole 232, through corrugated tubing 242 and drain pipe 252, and finally to a waste line #2 (not shown). As illustrated in Figures 1A through 1C, the two waste lines conveniently exit the device at the same location.

With the tiltable sink system of the present invention, the present invention can send different types of down different waste lines such that a first waste line may be used to remove nonhazardous waste and the other waste line may be used to remove hazardous waste. The non hazardous waste line may simply be connected to a sewage drain pipe. The hazardous waste line should be connected to hazardous waste container that is disposed of appropriately.

Figures 2A through 2C illustrate an alternate embodiment of a tiltable sink system. Referring to Figures 2A through 2C, the drain line travels straight down such that the two waste lines exit at different locations.

Fluid Flow components

Several other components are also located inside the autostainer. Figure 3 illustrates a conceptual diagram the fluid flow components of the autostainer. Referring to Figure 3, three different output devices located on the Z-Head assembly of the autostainer deliver air or fluid to the slides.

A first output device is the bulk fluid dispensing tube 321. The bulk fluid dispensing tube 321 is used to deliver relatively large

quantities of fluid to slides. The bulk fluid dispensing tube 321 may dispense buffer solution from buffer supply 301 or reagents from internal bulk reagent supplies 302, 303, and 304. The particular fluid dispensed is selected by 8-way distribution valve 331.

A second output device is the reagent-dispensing probe 322. The reagent-dispensing probe 322 draws in specific reagents using syringe pump 340 and then dispenses drawn-in reagents onto specific slides. To prevent contamination of the reagent-dispensing probe 322 from different reagents, the autostainer cleans the reagent-dispensing probe 322. Specifically, the autostainer first flushes the reagent dispensing probe 322 by forcing buffer solution through the reagent dispensing probe 322 using three-way valve 332. Then, the autostainer dries the reagent dispensing probe 322 by forcing air through the reagent dispensing probe 322 using three-way valve 333.

The third output device is air blade 323. Air blade 323 is used to dry off slides and blow away extra reagents.

Autostainer Reagent Packs

To simplify operation, the present invention introduces an autostainer system with greatly simplified operation. To use the autostainer system of the present invention, a user simply adds a set of slides where each slide is accompanied by a specific reagent pack that contains the reagents needed for a specific slide preparation protocol. The reagent pack further includes information that identifies the slide preparation protocol to be performed.

Figure 4a illustrates a first embodiment of a reagent pack that may be used with the autostainer system of the present invention. As illustrated in Figure 4a, the reagent pack comprises a container with a set of wells (401 to 406 in Figure 4a) for storing reagents. The container is sealed using a cover 410. The cover 410 may include an identification mark such as barcode 411 to identify the slide preparation protocol to be performed. The cover 410 protects and retains the reagents in the wells 401 to 406, yet the reagent dispensing probe 322 is able to puncture and access the reagents as needed.

The cover 410 may further include a second barcode identification sticker 420. The barcode identification sticker 420 can be placed directly onto a slide to be performed such that the autostainer will automatically know the slide preparation protocol to be performed.

Figure 4b illustrates an alternate embodiment of a reagent pack 490. In the alternate embodiment of Figure 4b, the identifiers 431 and 441 have been placed parallel to the line of wells 401 to 406. In yet another embodiment (not shown), a tiltable sink is created with four drain holes with one hole at each corner. In such an embodiment, four different waste systems may be used.

The autostainer system of the present invention is capable of handling many different slide preparation protocols that require different numbers of reagents. Figures 5a, 5b, and 5c illustrate different sized reagent packs for different protocols. Figure 5a illustrates a simply four reagent pack for simple slide preparations. Figure 5b illustrates the six-

reagent pack of Figure 4a. Figure 5c illustrates an eight-reagent pack for complex slide preparation protocols.

The autostainer will be used to perform large numbers of slide preparations. Each slide preparation requires a reagent pack. To simplify purchasing, reagent packs may be purchased in bulk packages. Figure 6a illustrates one possible bulk package where several reagent packs are sold in a perforated two-dimensional matrix of individual reagent packs. Figure 6b illustrates an alternate bulk package where several reagent packs are sold as a strip of connected of individual reagent packs.

Autostainer Slide Racks

The slide racks for the autostainer of the present invention have been designed for ease-of-use and maximum flexibility. Figure7a illustrates a front view of one possible slide rack that may be used in the autostainer of the present invention. The slide rack 700 has four slide positions such that the slide rack 700 can hold four slides 710. Other slide rack embodiments may hold more or less than four slides. The slides may be standard U.S. or international sized slides. The slide rack 700 further includes four reagent positions for storing reagent packs 720 associated with the adjacent slide positions. Figure 7b illustrates a back view of the slide rack 700.

Autostainer Control and Programming

As stated in the previous section, the autostainer is controlled by a computer system. In a present embodiment, the computer system is based on a standard Personal Computer (PC) motherboard with a PCI bus.

The computer system runs an autostainer control program to control the operation of the autostainer.

The autostainer control program is a sophisticated control program that implements many security, automatic slide protocol programming, control, and logging features. To fully describe the autostainer control program, this document will step through a sample use of the autostainer.

User Loading

To operate the autostainer, a user loads slide trays (as illustrated in Figures 7a and 7b) with slide specimens and associated reagent packs. In one embodiment, the user simply places the proper reagent pack in the reagent pack receptacle adjacent to the specimen slide to be prepared. In another embodiment, the user places an associated identifier on the frosted area of the specimen slide to be prepared. This can be done by peeling off a barcode sticker 420 from the reagent pack 400 and placing it on the frosted area of the slide. By specifically labeling each slide with the protocol to be performed, no error can be introduced by accidentally placing the wrong reagent pack next to a specimen slide.

Slide Preparation Protocol Identification

After loading one or more slide trays, the user places the loaded slide trays into the autostainer system. The user then instructs the autostainer system to commence slide preparation by activating a "restart" input. If the user has added very high priority slides to the autostainer, the user may instead press a "STAT" input to indicate that the new slides are

very high priority. The autostainer system then commences operation by first examining the loaded slides and reagent packs to determine the slide preparation protocols that need to be performed. Specifically, the autostainer system reads all the identifiers (on the slides and/or reagent packs) and then consults a slide preparation protocol database that maps the different identifiers on the reagent packs with the slide preparation protocols to be performed.

The slide preparation protocol database may be periodically updated by shipping media such as floppy disks or CD-ROMs that are inserted into an appropriate drive on the autostainer. In one embodiment, the autostainer system uses a network to automatically retrieve database updates. This may be performed by having the autostainer coupled to a telephone line with a modem such that the autostainer automatically calls specific number to obtain slide preparation protocol database updates. In an alternate embodiment, the autostainer may be coupled to the global Internet such that the autostainer may connect to a server that stores the most recent slide preparation protocol database information. In any of these embodiments, the autostainer may also simultaneously receive program updates such that the software that controls the autostainer may be automatically updated.

Slide Staining Apparatus Operation

Once a user has loaded the autostaining apparatus, the user may start staining run. Figure 8A illustrates the general procedure of operating the autostaining device. Referring to Figure 8A, the user loads a

slide/stain tray at step 801. The user then starts the apparatus by pressing the restart or stat button at step 802. The autostaining apparatus then examines all the slides to determine the slide protocols that must be performed at step 803. The system may compare a barcode sticker 402 on a slide with a barcode 411 on the cover 410 of an adjacent reagent pack to ensure that the proper reagent pack has been placed next to each slide. After examining all the slides and reagent packs, the system creates a staining schedule. Details on how the staining apparatus creates the staining schedule will be presented in the following section.

After calculating a staining schedule, the autostaining apparatus beings to process slides according to a created staining schedule. The system continues the staining operations until one of the conditions of step 805 are detected (or an error occurs). Specifically, step 805 determines if the staining run is completely done, the staining run is partially done, or if the user has pressed the pause button.

If the staining run is partially done, then the system proceeds to step 807 where the user is informed of the completed slide(s). The user may wish to remove those slides such that they can be examined.

If the user pressed the pause button, then the system temporarily ceases operation. The user may then load additional slide trays at step 801. The system remains paused as it waits for the user to press the restart or stat button. Once the user has pressed either the restart or stat button at step 802, the system proceeds to step 803 to create a new

staining schedule. The system then resumes slide staining at step 804 using the new staining schedule.

Referring back to step 805, if the system is completely done with the staining run, then the system may cease operation. As shown in Figure 8A, a user may continually remove completed slide trays and add new slide trays continually by only using the pause and restart/stat buttons. Thus, the staining apparatus may be in continuous operation all day long.

Slide Preparation Scheduling

Once the slide preparation protocols that need to be performed have been identified, the autostainer control program proceeds to calculate the most efficient dispensing pattern for performing the desired slide protocols.

Figure 8B illustrates a summary of how the autostainer control program calculates the most efficient dispensing pattern. Referring to Figure 8B, at step 810 the autostainer control program first determines if a run was already in progress. If a run was already in progress, then the autostainer control program adds the current slides into a scheduling table at step 815. The scheduling table will be used to program the autostainer control program.

Next, at step 820, the autostainer control program has the z-head assembly scan all the slide positions to determine if any new slides have been added or any existing slides have been taken away. If a slide that had not yet completed its protocol was removed, the autostainer may inform the user of the error and ask if the user wishes to place the slide

back into the autostainer. When one or more new slides have been added, the autostainer control program adds those slides into the current scheduling table as stated in step 820 of Figure 8B. If the user designated the new slides as "STAT", then those newly added slides are given top priority.

After the autostainer control program has added the filled the scheduling table, the autostainer control program proceeds to step 830 to begin automatic programming. At step 830, the autostainer control program first places the slides into a specific order. In one embodiment, the autostainer control program orders the slides using this order:

1. Highest priority slides (such as STAT slides).
2. Slides with the longest incubation time.
3. Numerical order.

The system then proceeds to re-order the slides using a well-defined method. Figure 8B illustrates one possible method of ordering the slides. Initially, the first slide from the order of step 830 defines the currently scheduled array (CSA). The CSA defines a newly proposed slide order. At step 845, the method selects the next unscheduled slide from the scheduling table. That slide is then placed into the CSA as stated in step 850. At step 860, the method determines if the slide fit properly into the current stage of the CSA. The method of determining if a slide "fits" into the current stage of the CSA is fully defined in Figures 9a to 9d. If the slide did not fit, the method proceeds to step 870 to determine if the control program has tried to fit all the remaining unscheduled slides into the current

stage. If there are unscheduled slides that the autostainer control program has not attempted to put into the current stage, then the method proceeds to step 873 to select an unscheduled slide with a different protocol. The autostainer control program then returns to step 850 to attempt to add that slide into the current stage.

If, at step 870, the autostainer control program is unable to fit any unscheduled slide into the current stage, then the autostainer control program move to the next stage of the current schedule array (CSA) as stated in step 879. The autostainer control program then proceeds back to step 845 to start placing slides into the new stage.

Referring back to step 860, after each new slide is added to the CSA, the autostainer control program determines if all the slides have been scheduled as stated in step 880. If all the slides have been scheduled, the autostainer control program determines if it has created a slide-processing schedule that is faster than the current best time. If the autostainer control program determines that it created a slide-processing schedule faster than the previous best time, then the autostainer control program saves the newly created schedule as the best schedule at step 883. At step 890, the autostainer control program determines if it has tried all the possible slide orders. If it has not, the autostainer control program proceeds to step 895 where the autostainer control program changes the slide order while maintaining the designated slide priority order. The autostainer control program then proceeds back to step 840 to test a new slide schedule. If, at step 890, the autostainer control program determines

that it has tried every possible slide order (that maintains the slide priority order), the autostainer control program returns the best schedule.

The foregoing has described a method and apparatus for automatic tissue and cell preparation staining. It is contemplated that changes and modifications may be made by one of ordinary skill in the art, to the materials and arrangements of elements of the present invention without departing from the scope of the invention.

What is claimed is:

1. A method of operating an autostainer device, said method comprising the steps of:

accepting a slide tray, said slide tray having at least one specimen slide and a reagent pack associated with said specimen slide, said reagent pack comprising a first identifier that specifies a particular slide preparation protocol;

reading said first identifier from said reagent pack; and

preparing said specimen slide according to said particular slide preparation protocol.

2. The method as claimed in claim 1 wherein said reagent pack is associated with said specimen slide by being adjacent to said specimen slide.

3. The method as claimed in claim 1 wherein said reagent pack is associated with said specimen slide by having a second identifier on said specimen slide that is the same as said first identifier.

4. The method as claimed in claim 1 wherein said reagent pack comprises a set of wells, each well containing a reagent needed for said particular slide preparation protocol.

5. The method as claimed in claim 1 wherein said reagent pack comprises a peel-off identifier, said peel-off identifier for placement on said specimen slide.

6. A method of operating an autostainer device, said method comprising the steps of:

accepting a slide tray, said slide tray having at least one specimen slide and a reagent pack associated with said specimen slide, said specimen slide comprising a first identifier that specifies a particular slide preparation protocol for said specimen slide;

reading said first identifier; and

preparing said specimen slide according to said particular slide preparation protocol.

7. The method as claimed in claim 6 wherein said reagent pack is associated with said specimen slide by being adjacent to said specimen slide.

8. The method as claimed in claim 6 wherein said reagent pack is associated with said specimen slide by having a second identifier that is the same as said first identifier.

9. The method as claimed in claim 6 wherein said reagent pack comprises a set of wells, each well containing a reagent needed for said particular slide preparation protocol.

10. The method as claimed in claim 6 wherein said reagent pack comprises a peel-off identifier containing said first identifier, said peel-off identifier for placement on said specimen slide.

11. An apparatus for staining specimen slides, said apparatus comprising:

more than one slide tray, said slide tray for holding more than one specimen slide;

an automatic staining head assembly, said automatic staining head assembly for depositing reagents on said specimen slides, said automatic staining head assembly further comprising an input device for reading identifiers that specify slide preparation protocols to perform;

a control system, said control system coupled to said automatic staining head assembly for controlling said automatic staining head assembly to prepare said specimen slides during a staining run;

a pause input, said pause input for pausing said apparatus during said staining run; and

a restart input, said restart input for restarting said apparatus after adding new specimen slides onto on of said slide trays;

wherein said control system causes said automatic staining head assembly to read a new set of identifiers associated with said new specimen slides to add said new specimen slides to said staining run.

12. The apparatus as claimed in claim 11 wherein said apparatus further comprises reagent packs.

13. The apparatus as claimed in claim 12 wherein each said reagent pack comprises a set of wells, each well containing a reagent needed for said particular slide preparation protocol.

14. The apparatus as claimed in claim 12 wherein said identifiers comprise a barcode on each said reagent pack.

15. The apparatus as claimed in claim 11 wherein said identifiers comprise a set of barcodes on said specimen slides.

16. The apparatus as claimed in claim 11 further comprising:

a STAT restart input, said STAT restart input for restarting said apparatus after adding new specimen slides onto on of said slide trays wherein said new specimen slides are given high priority;

17. A slide rack for a slide staining apparatus, said slide rack comprising:

a first receptacle for accepting a specimen slide; and

a second receptacle for accepting a reagent pack, said reagent pack containing at least one reagent needed to prepare said specimen slide.

18. The slide rack as claimed in claim 17 further wherein said reagent pack further comprises an identifier that identifies a slide preparation protocol for said specimen slide.

19. The slide rack as claimed in claim 17 further wherein said first receptacle and said second receptacle are adjacent to each other.

20. A reagent pack for a slide staining apparatus, said reagent pack comprising:

a set of wells, said well containing reagents for a specific slide preparation protocol; and

an identifier, said identifier associated with said slide preparation protocol.

21. The reagent pack as claimed in claim 20 wherein said identifier comprises a peel-off sticker for placement on an associated specimen slide.

22. The reagent pack as claimed in claim 20 further wherein said identifier comprises a peel-off sticker for placement on an associated specimen slide.

23. A slide staining apparatus, said apparatus comprising:

at least one slide rack for holding a slide specimen to be prepared; and

a tiltable sink assembly, said tiltable sink assembly having a first drain hole on a first side such that liquid material drains through said first drain hole when tilted down on said first side, said tiltable sink assembly having a second drain hole on a second side such that liquid material drains through said second drain hole when tilted down on said second side.

24. The apparatus as claimed in claim 23 wherein said first drain hole is coupled to a sewage system.

25. The apparatus as claimed in claim 23 wherein said second drain hole is coupled to a hazardous waste container.

26. The apparatus as claimed in claim 23 wherein said second drain hole is coupled to a corrugated tube.

27. An apparatus for staining specimen slides, said apparatus comprising:

at least one slide tray, said slide tray for holding at least one specimen slide and an associated reagent pack, said associated reagent pack having reagents needed for processing said specimen slide; and

an automatic staining head assembly, said automatic staining head assembly for obtaining said reagents from said associated reagent pack and depositing reagents on said specimen slide.

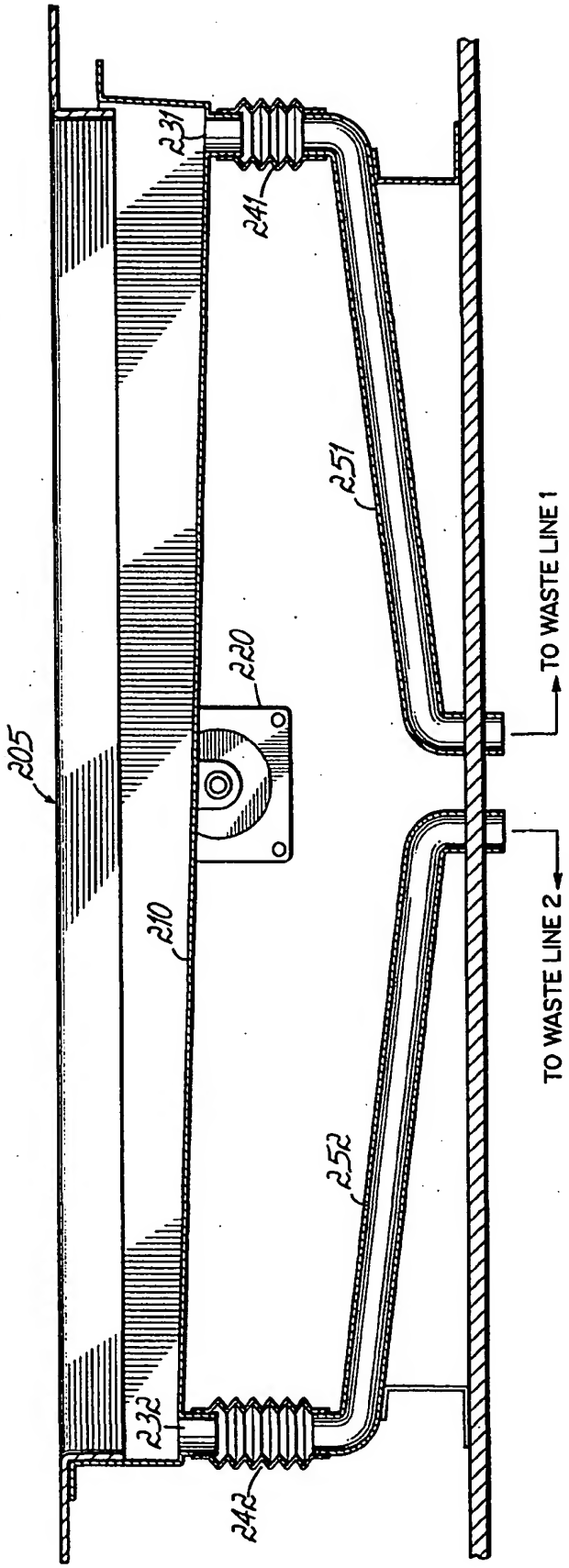

231
241
251
220
205
210
232
242
252
TO WASTE LINE 1
TO WASTE LINE 2

FIG. 1A

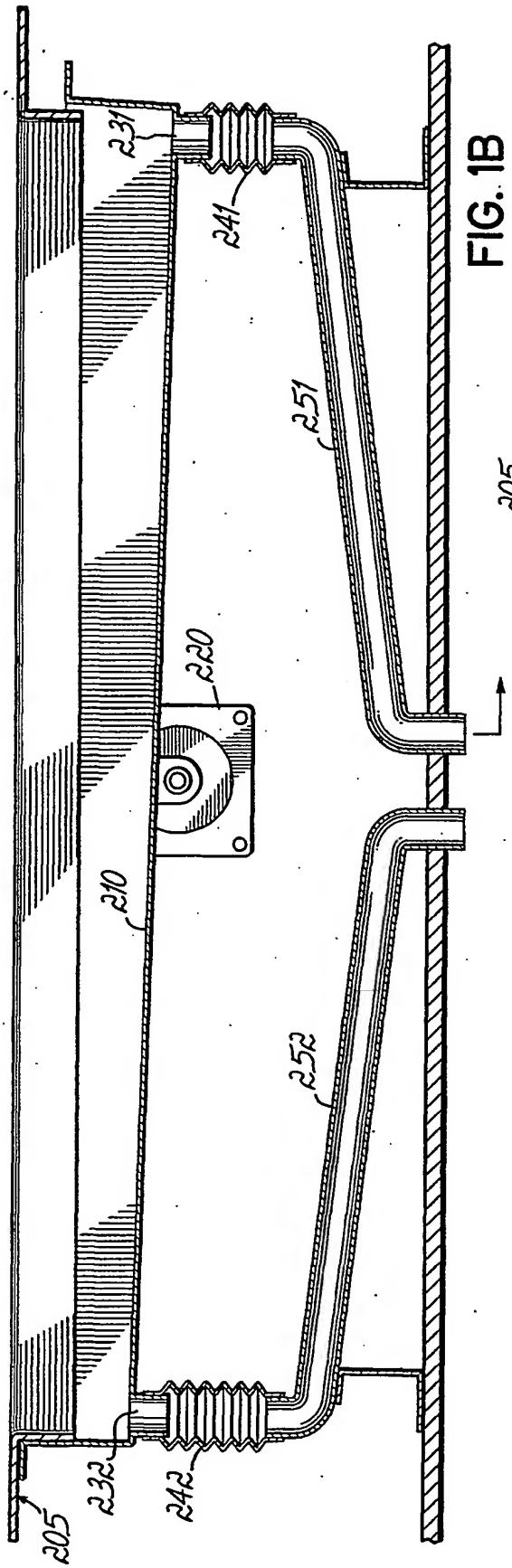
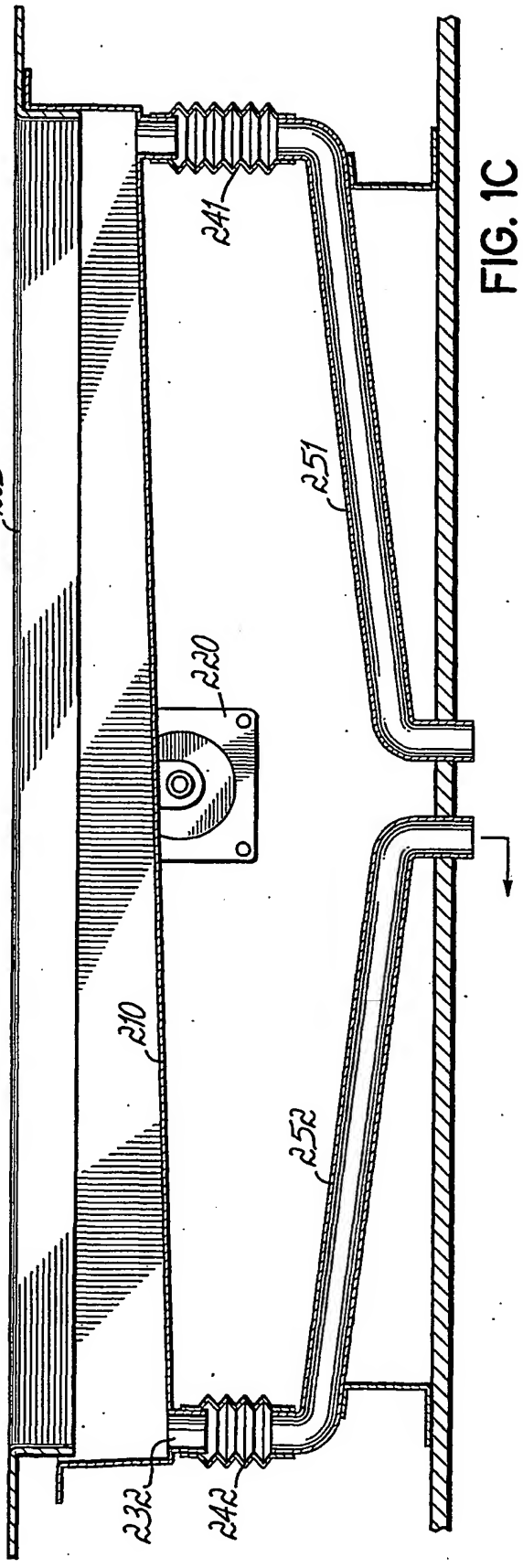

231
241
251
220
210
252
232
242
205

FIG. 1B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220
210
252
232
242

FIG. 1C

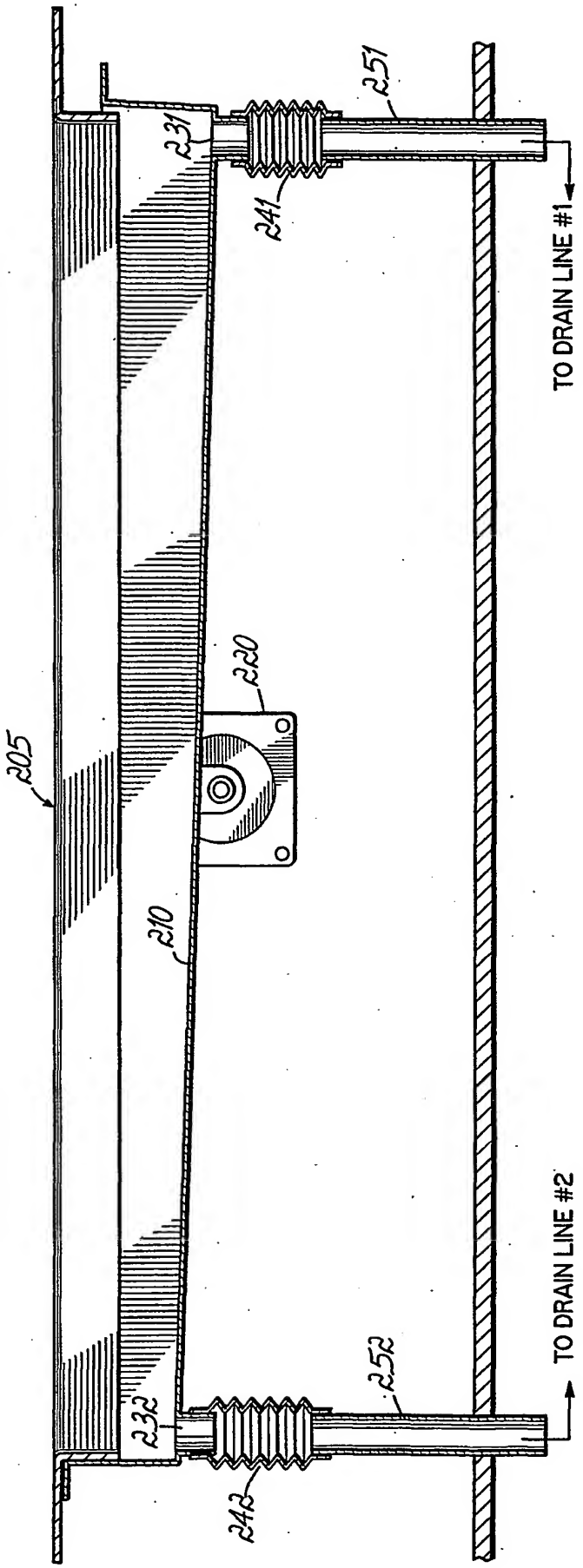
251
231
241
TO DRAIN LINE #1
220
205
210
TO DRAIN LINE #2
252
232
243

FIG. 2A

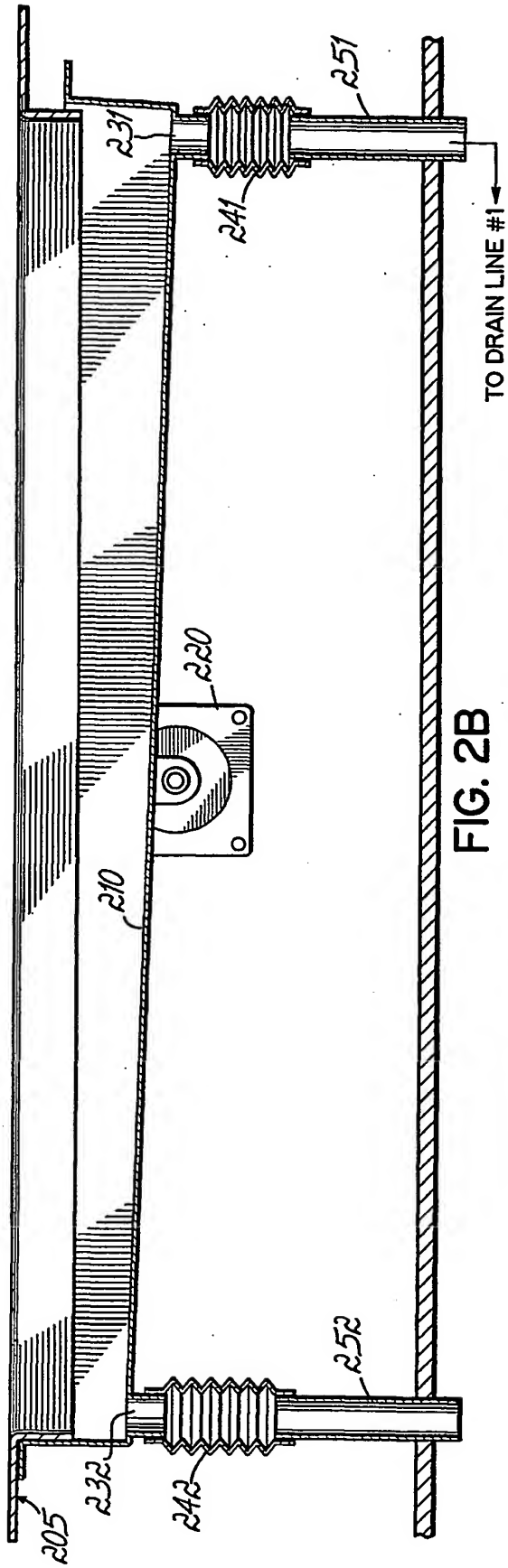
231
251
241
TO DRAIN LINE #1
220
210
252
232
242
205

FIG. 2B

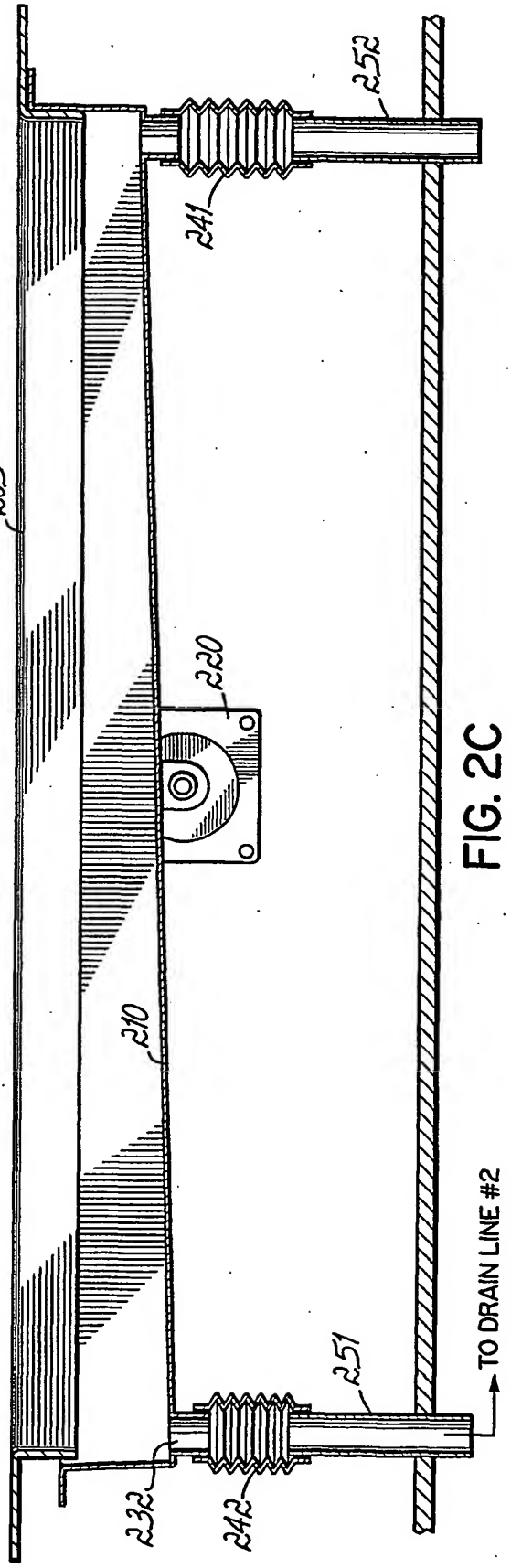
252
241
205
220
210
232
242
251
TO DRAIN LINE #2

FIG. 2C

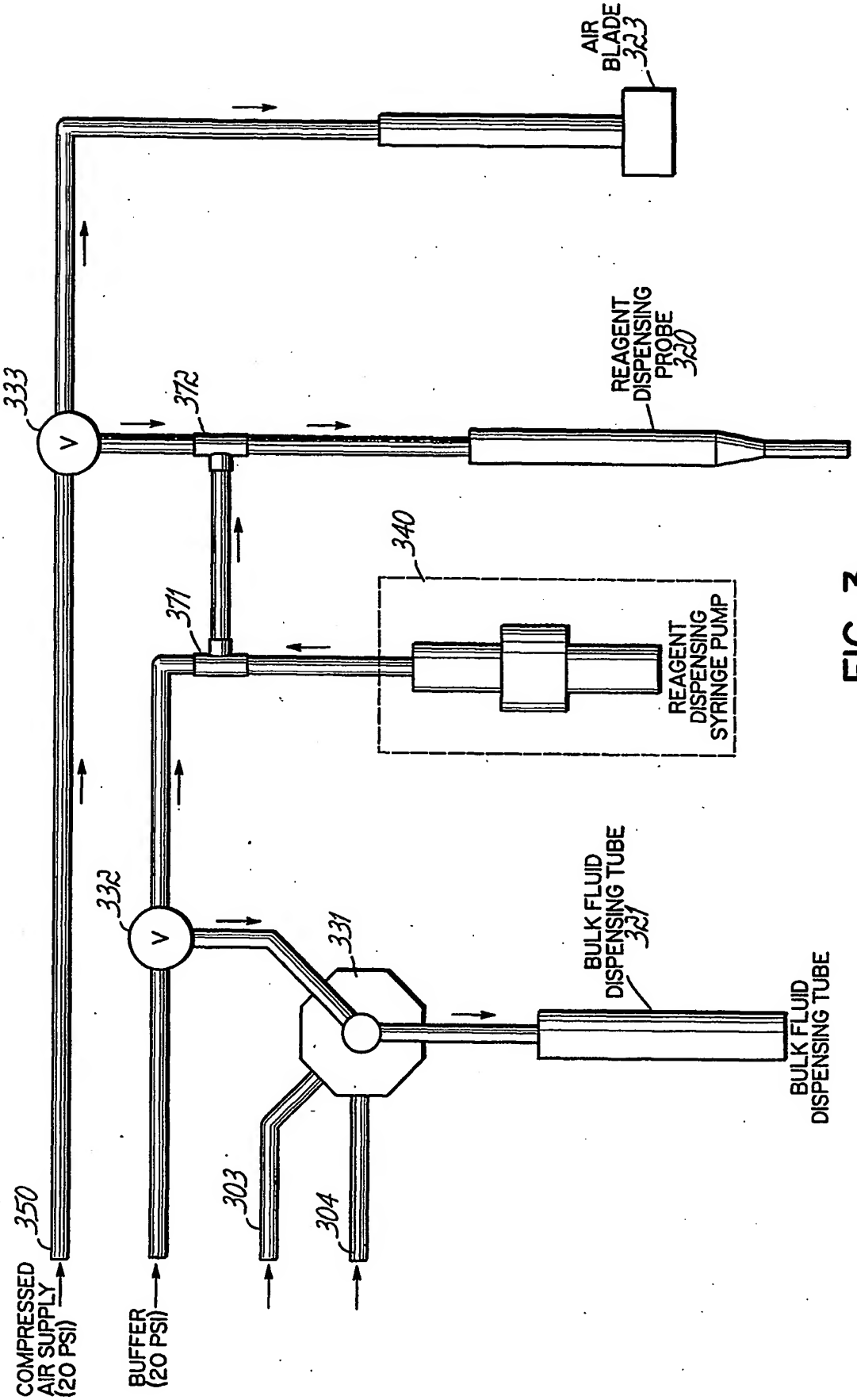
AIR BLADE 323
REAGENT DISPENSING PROBE 320
333
372
340
371
REAGENT DISPENSING SYRINGE PUMP
332
331
BULK FLUID DISPENSING TUBE 321
BULK FLUID DISPENSING TUBE
350
303
304
COMPRESSED AIR SUPPLY (20 PSI)
BUFFER (20 PSI)

FIG. 3

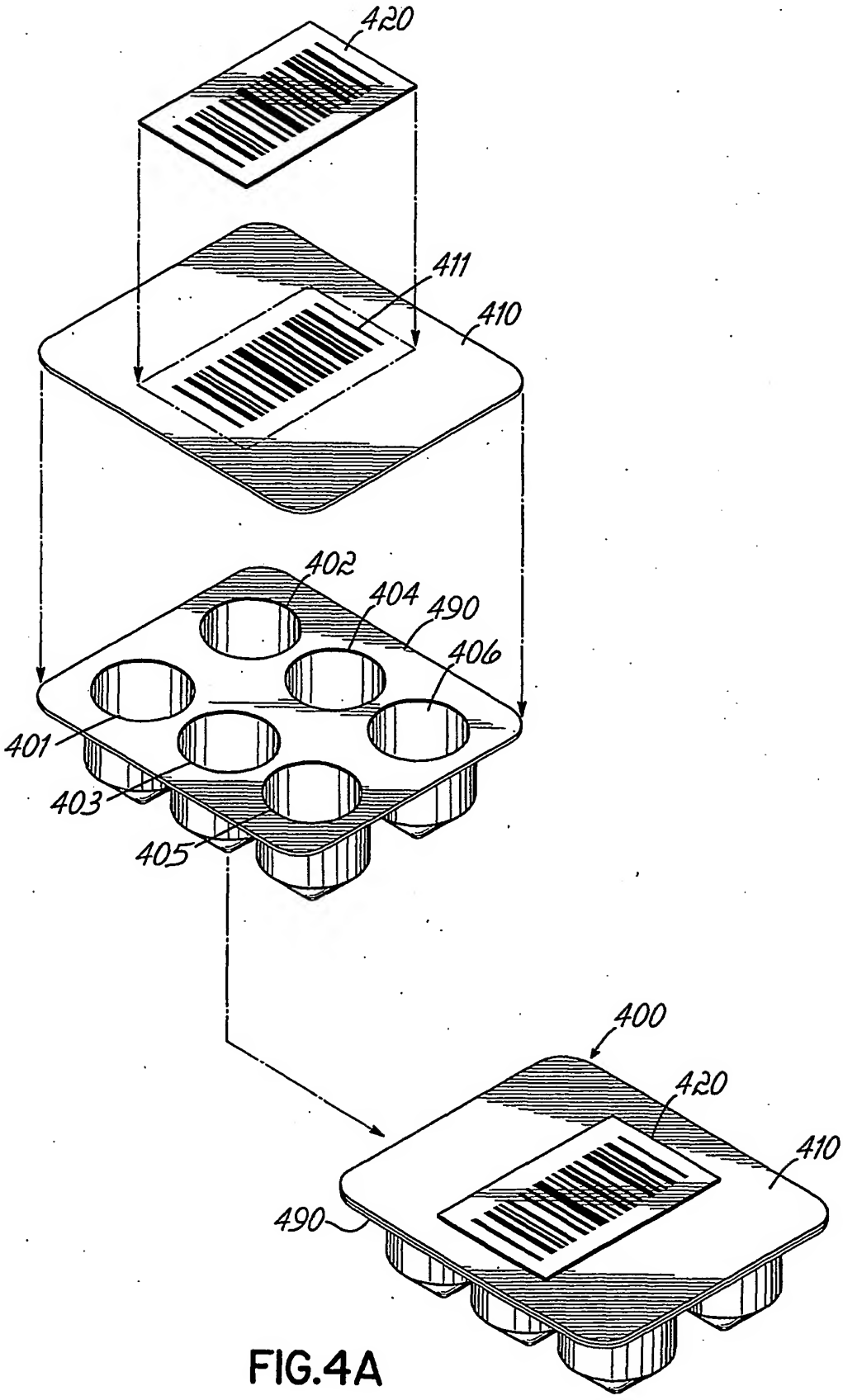

FIG.4A

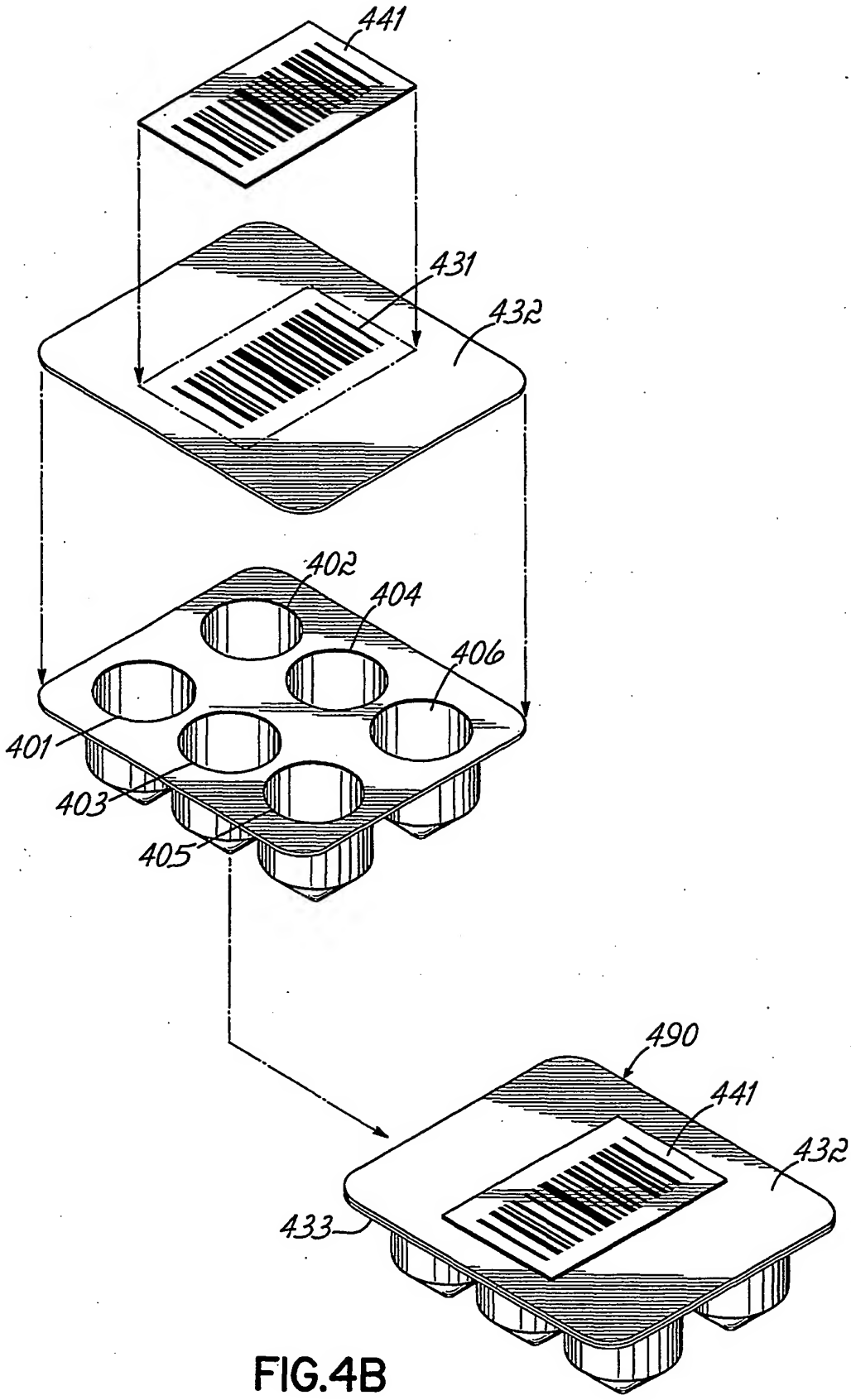

FIG.4B

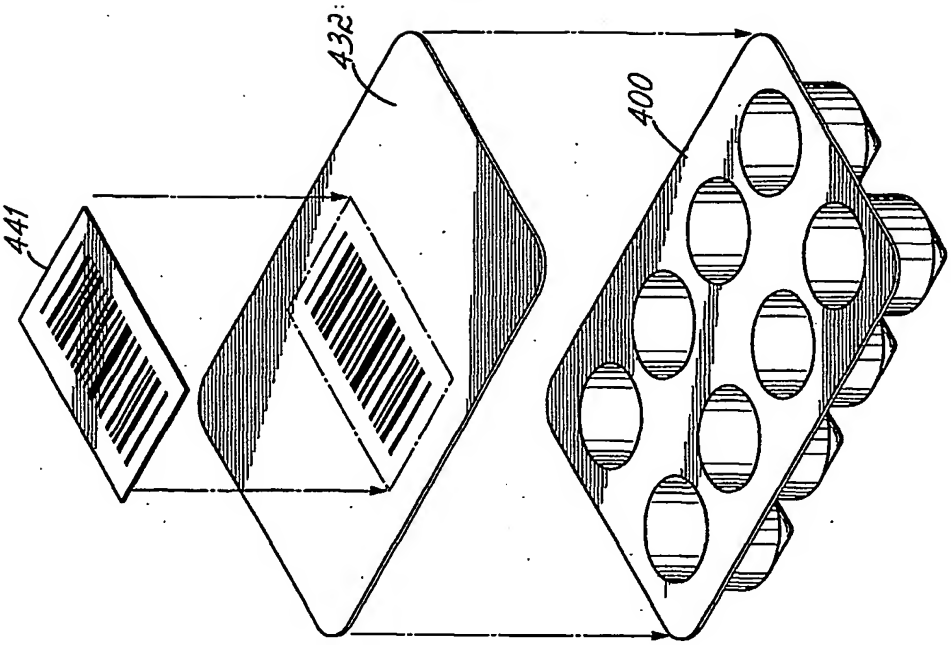

FIG. 5C

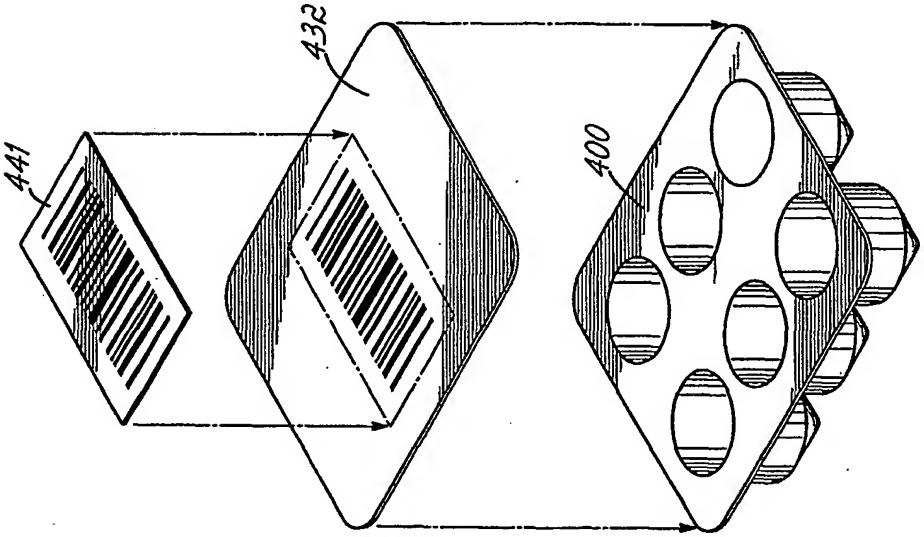

FIG. 5B

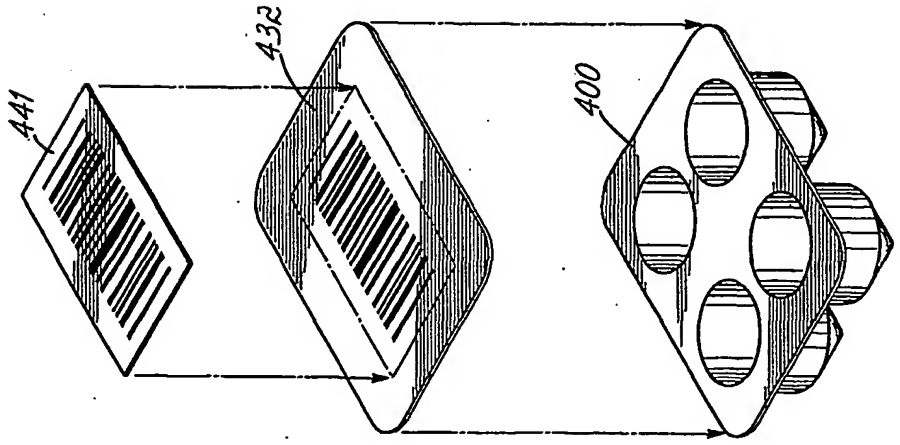

FIG. 5A

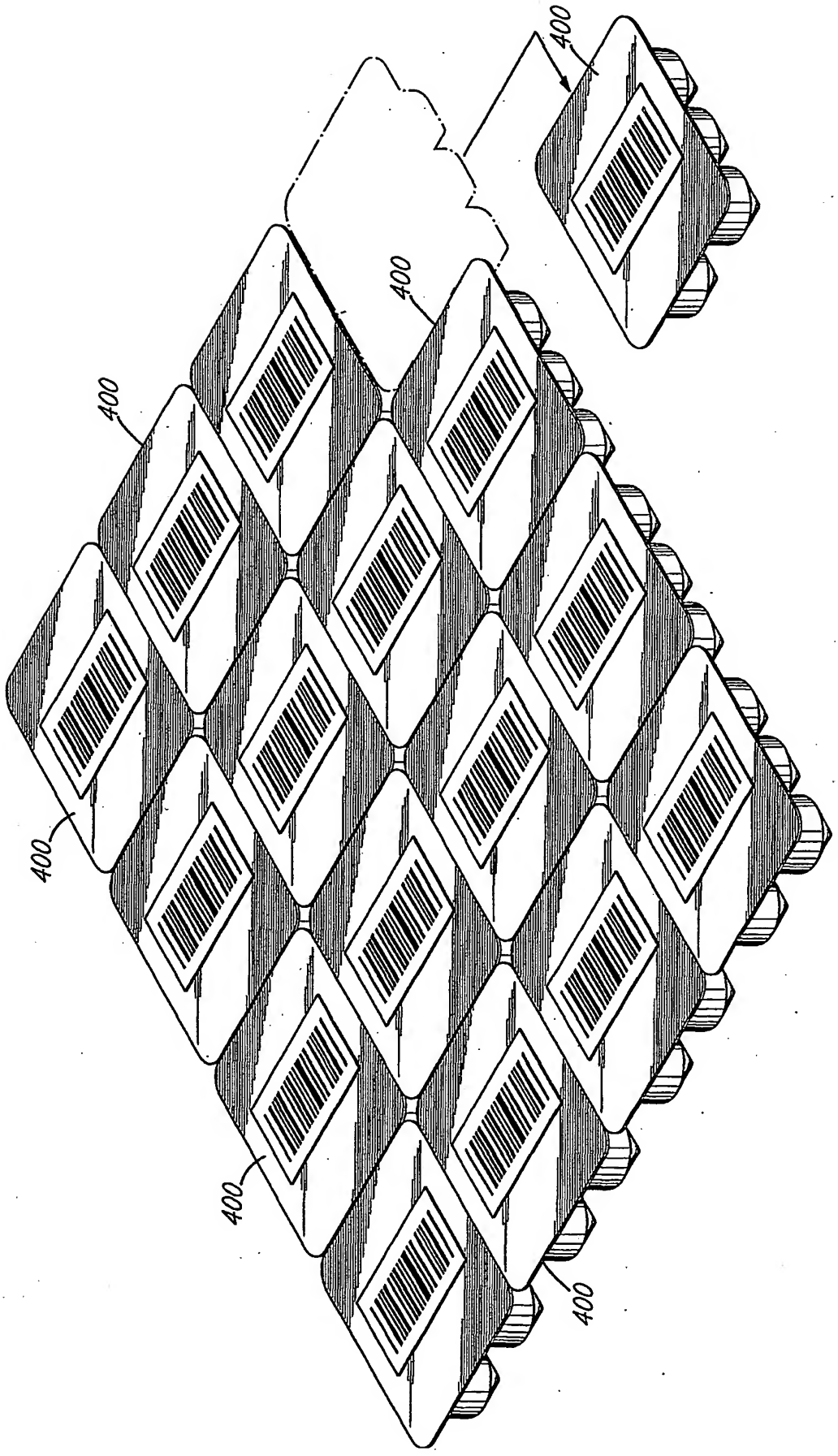

FIG. 6A

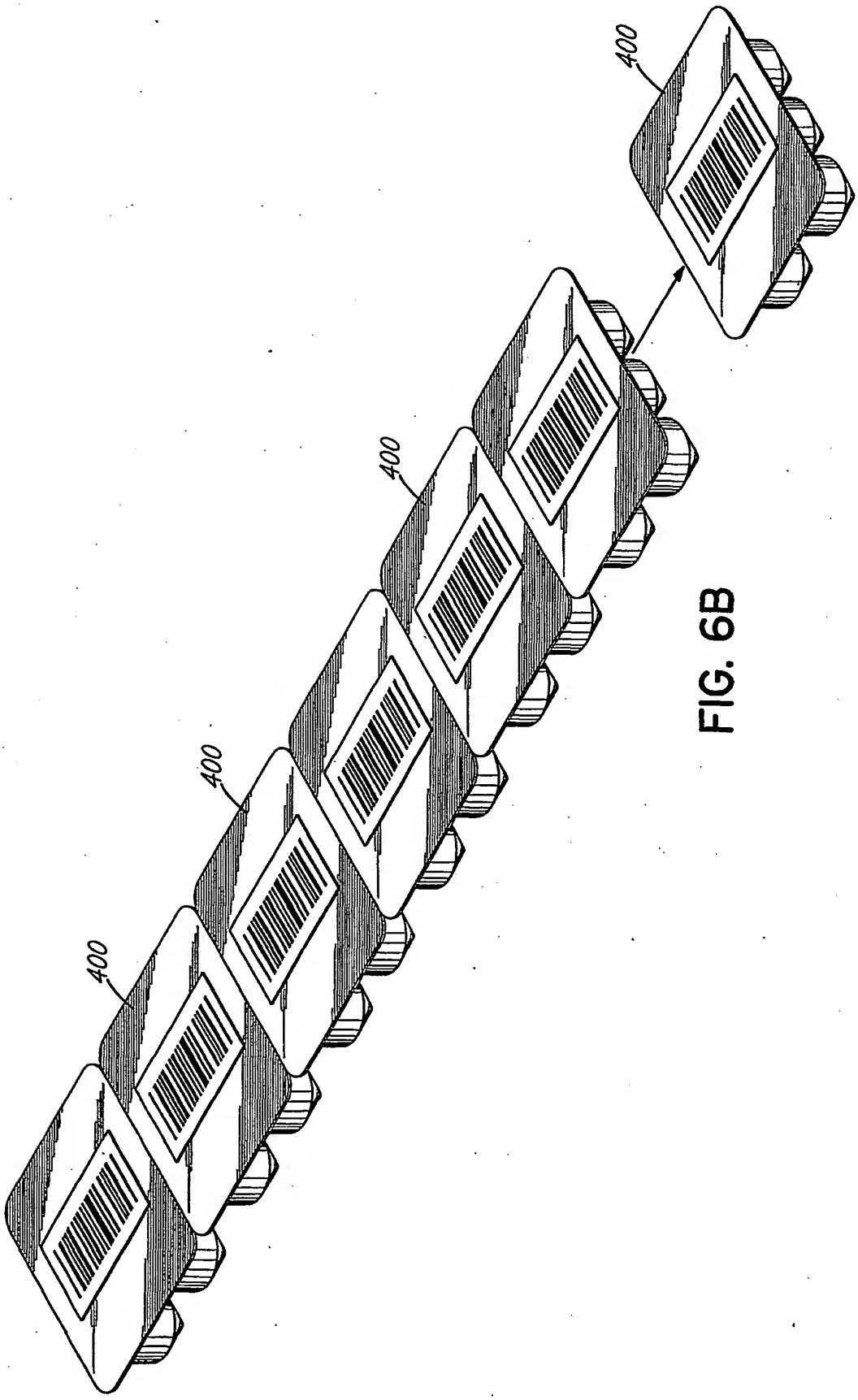

FIG. 6B

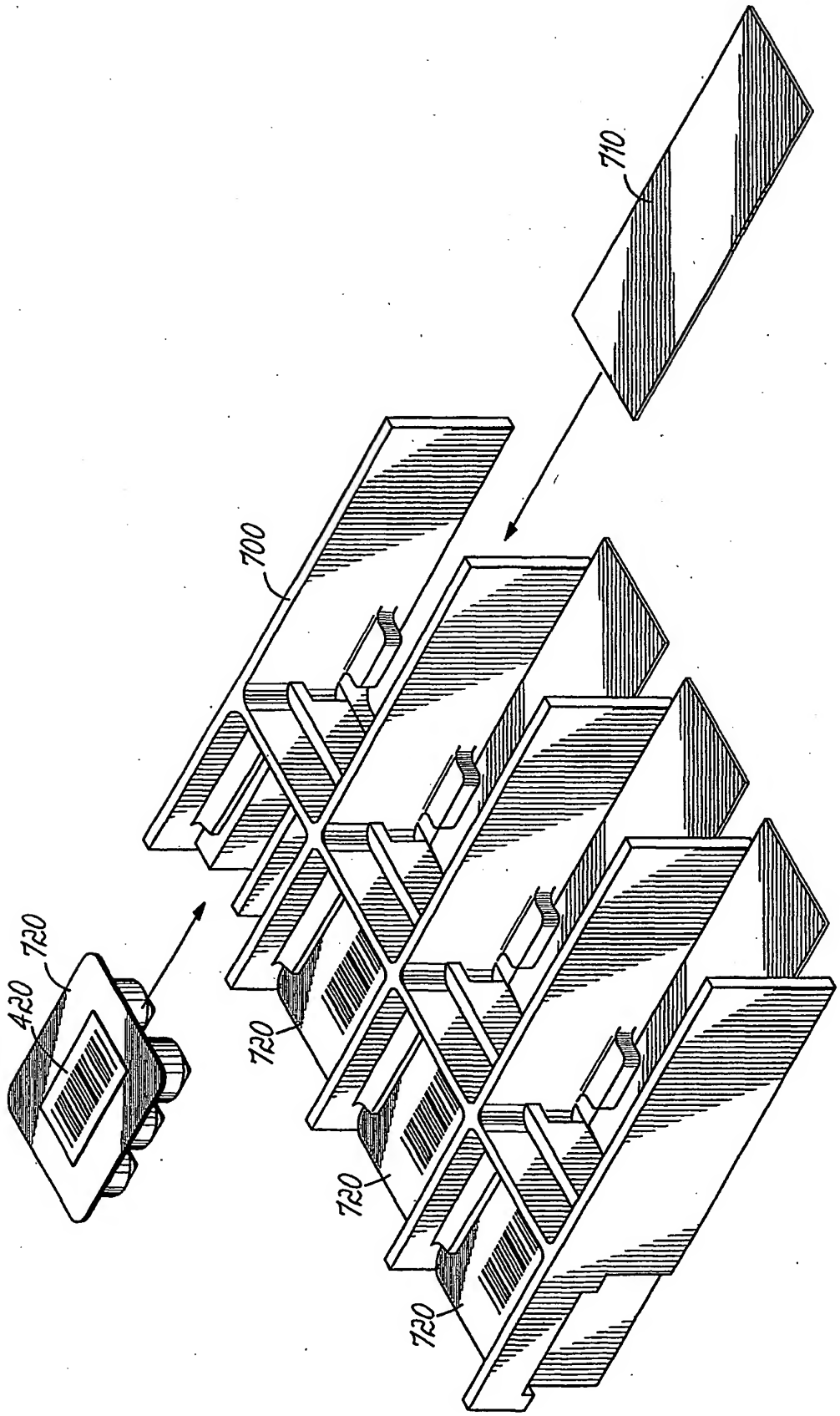

FIG.7A

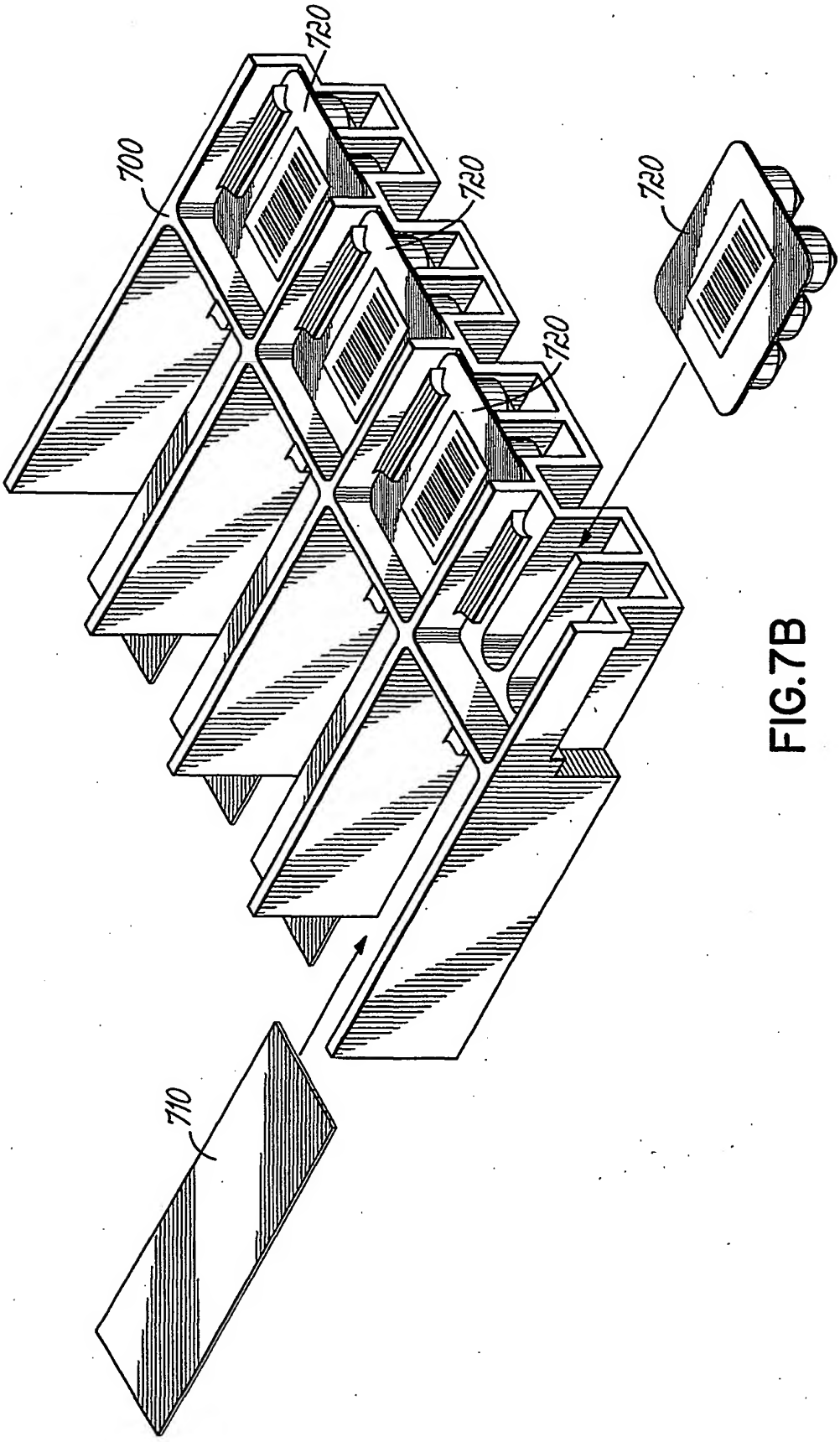

FIG.7B

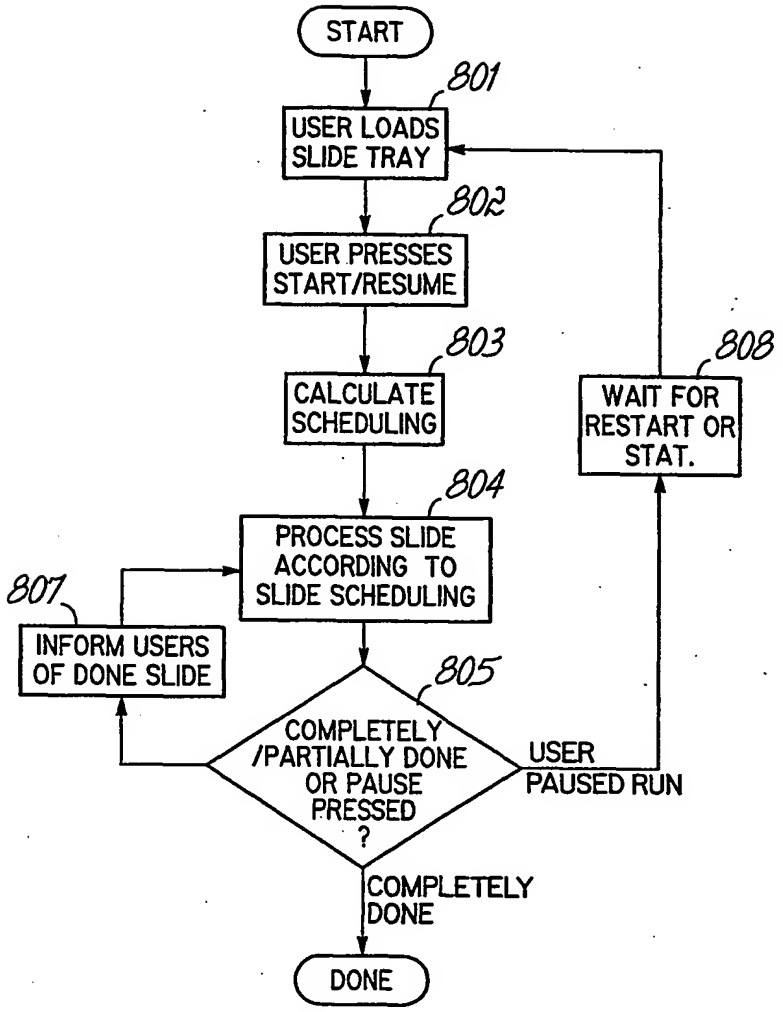
START
801
USER LOADS SLIDE TRAY
802
USER PRESSES START/RESUME
803
CALCULATE SCHEDULING
804
PROCESS SLIDE ACCORDING TO SLIDE SCHEDULING
805
COMPLETELY /PARTIALLY DONE OR PAUSE PRESSED ?
USER PAUSED RUN
807
INFORM USERS OF DONE SLIDE
808
WAIT FOR RESTART OR STAT.
COMPLETELY DONE
DONE

FIG. 8A

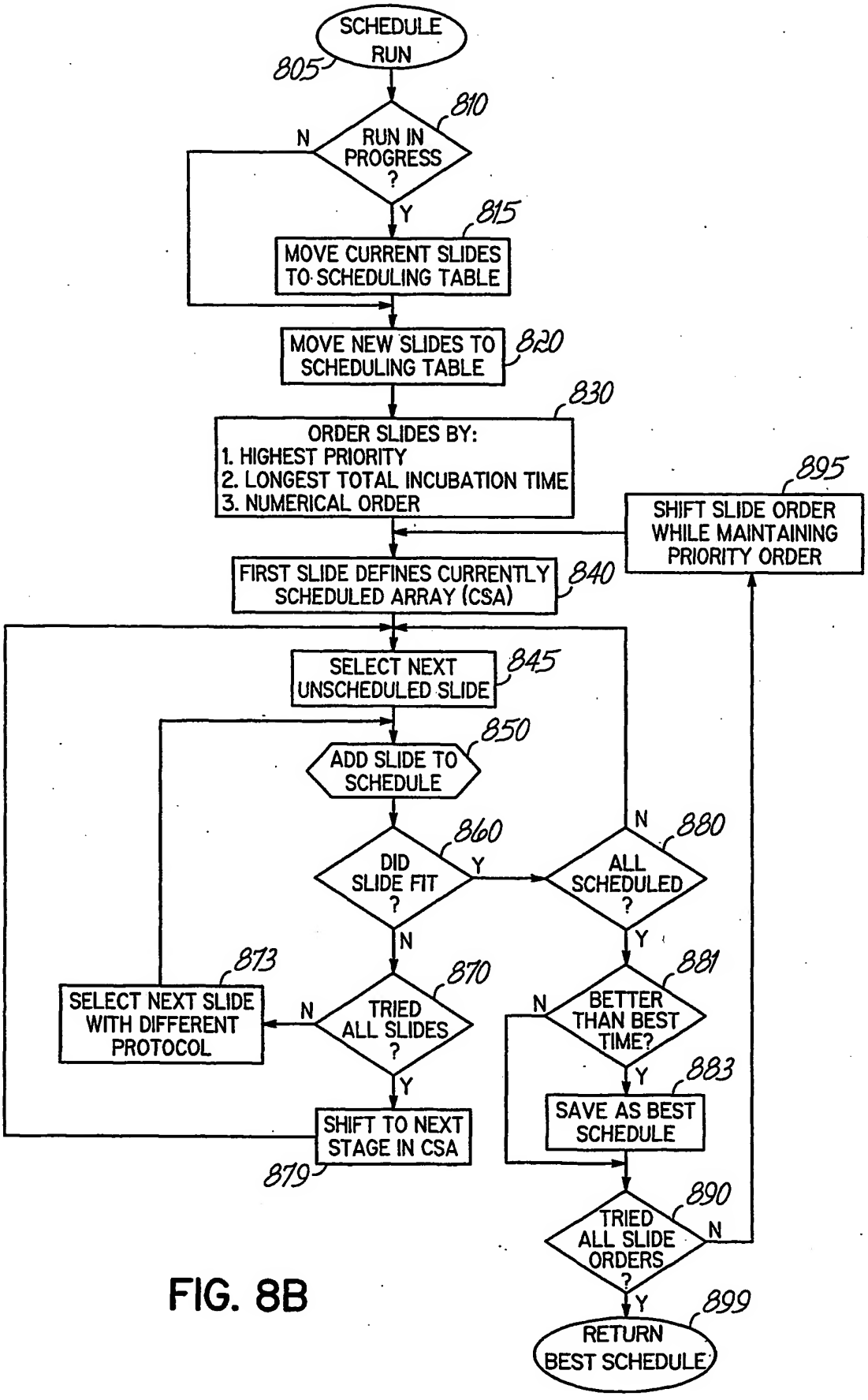
SCHEDULE RUN
805
RUN IN PROGRESS ?
810
N
Y
MOVE CURRENT SLIDES TO SCHEDULING TABLE
815
MOVE NEW SLIDES TO SCHEDULING TABLE
820
ORDER SLIDES BY:
1. HIGHEST PRIORITY
2. LONGEST TOTAL INCUBATION TIME
3. NUMERICAL ORDER
830
SHIFT SLIDE ORDER WHILE MAINTAINING PRIORITY ORDER
895
FIRST SLIDE DEFINES CURRENTLY SCHEDULED ARRAY (CSA)
840
SELECT NEXT UNSCHEDULED SLIDE
845
ADD SLIDE TO SCHEDULE
850
DID SLIDE FIT ?
860
Y
N
ALL SCHEDULED ?
880
N
Y
SELECT NEXT SLIDE WITH DIFFERENT PROTOCOL
873
TRIED ALL SLIDES ?
870
N
Y
BETTER THAN BEST TIME?
881
N
Y
SAVE AS BEST SCHEDULE
883
SHIFT TO NEXT STAGE IN CSA
879
TRIED ALL SLIDE ORDERS ?
890
N
Y
RETURN BEST SCHEDULE
899

FIG. 8B

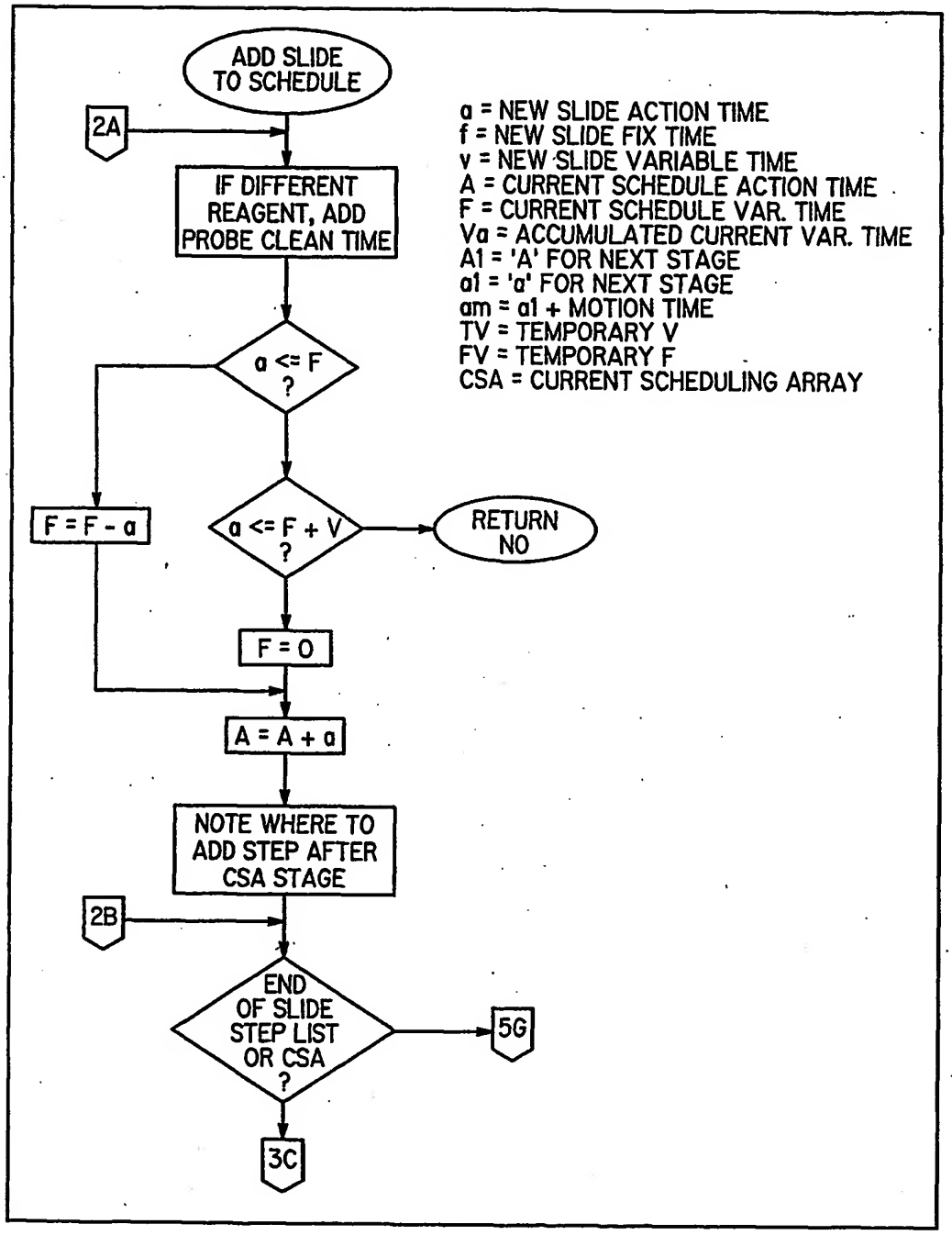
ADD SLIDE TO SCHEDULE
2A
IF DIFFERENT REAGENT, ADD PROBE CLEAN TIME
a <= F ?
F = F - a
a <= F + V ?
RETURN NO
F = 0
A = A + a
NOTE WHERE TO ADD STEP AFTER CSA STAGE
2B
END OF SLIDE STEP LIST OR CSA ?
5G
3C
a = NEW SLIDE ACTION TIME
f = NEW SLIDE FIX TIME
v = NEW SLIDE VARIABLE TIME
A = CURRENT SCHEDULE ACTION TIME
F = CURRENT SCHEDULE VAR. TIME
Va = ACCUMULATED CURRENT VAR. TIME
A1 = 'A' FOR NEXT STAGE
a1 = 'a' FOR NEXT STAGE
am = a1 + MOTION TIME
TV = TEMPORARY V
FV = TEMPORARY F
CSA = CURRENT SCHEDULING ARRAY

FIG. 9A

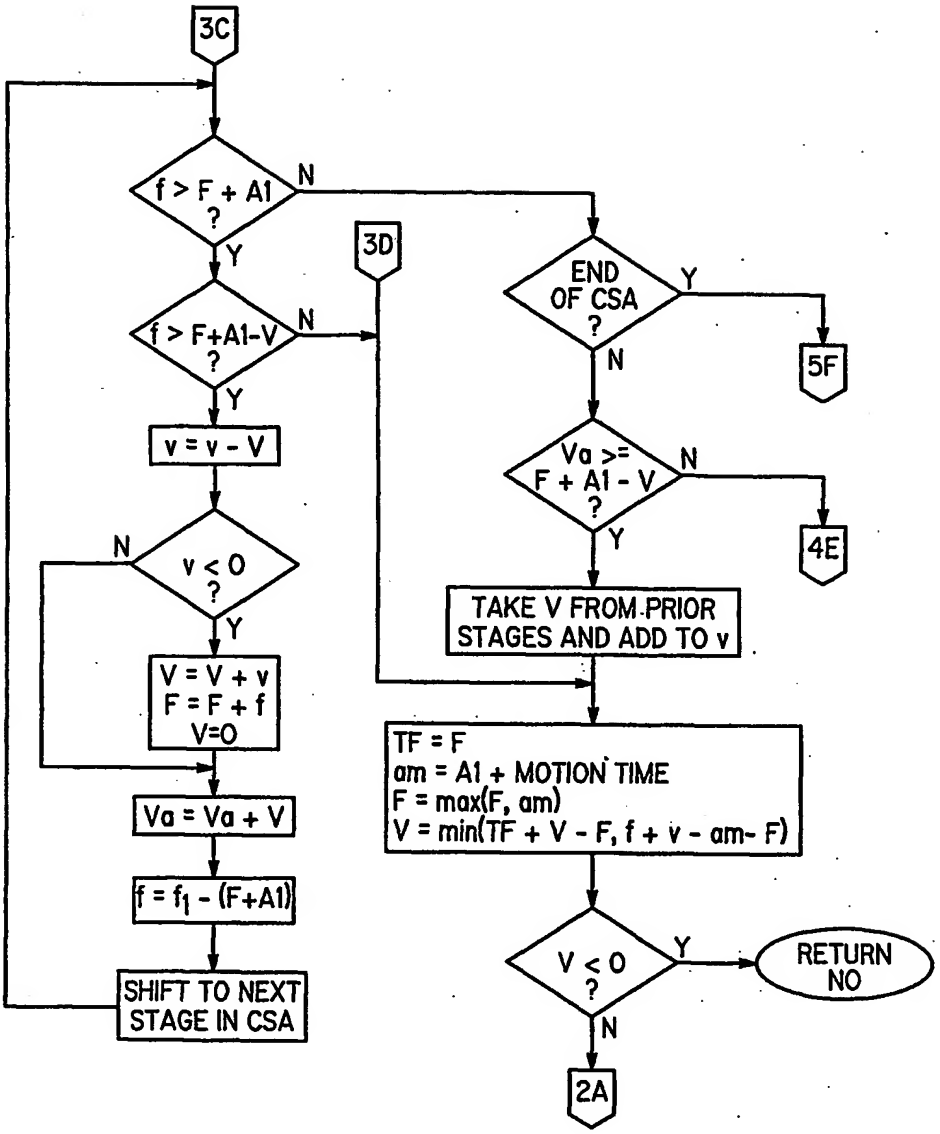
3C
f > F + A1 ?
N
Y
f > F+A1-V ?
N
Y
v = v - V
N
v < 0 ?
Y
V = V + v
F = F + f
V=0
Va = Va + V
f = f1 - (F+A1)
SHIFT TO NEXT STAGE IN CSA
3D
END OF CSA ?
Y
5F
N
Va >= F + A1 - V ?
N
4E
Y
TAKE V FROM PRIOR STAGES AND ADD TO v
TF = F
am = A1 + MOTION TIME
F = max(F, am)
V = min(TF + V - F, f + v - am- F)
V < 0 ?
Y
RETURN NO
N
2A

FIG. 9B

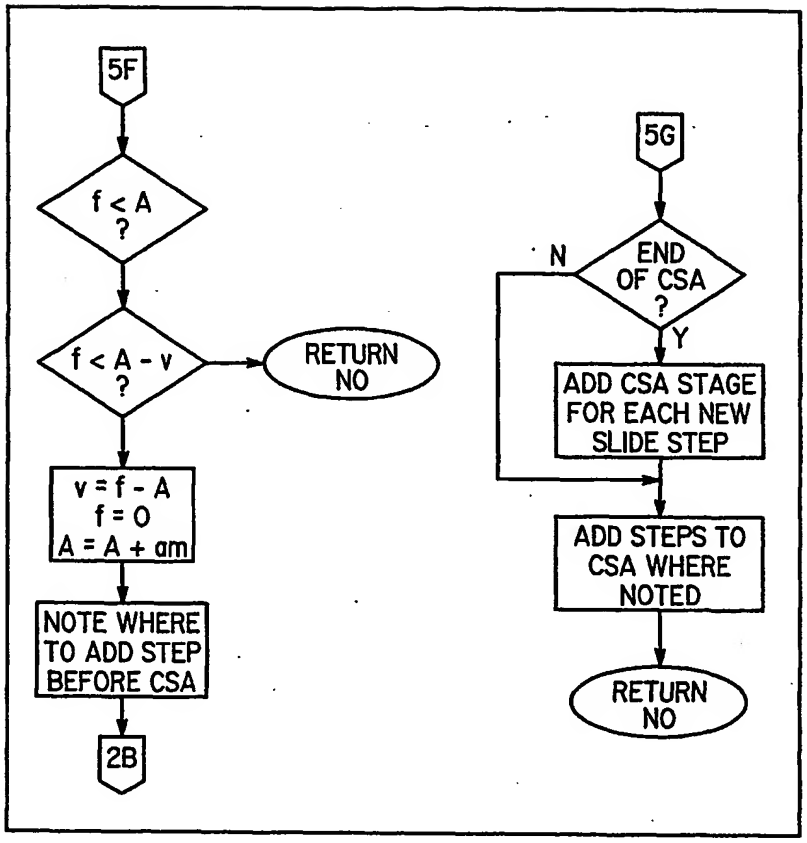
5F
f < A ?
f < A - v ?
RETURN NO
v = f - A
f = 0
A = A + am
NOTE WHERE TO ADD STEP BEFORE CSA
2B
5G
N
END OF CSA ?
Y
ADD CSA STAGE FOR EACH NEW SLIDE STEP
ADD STEPS TO CSA WHERE NOTED
RETURN NO

FIG. 9D

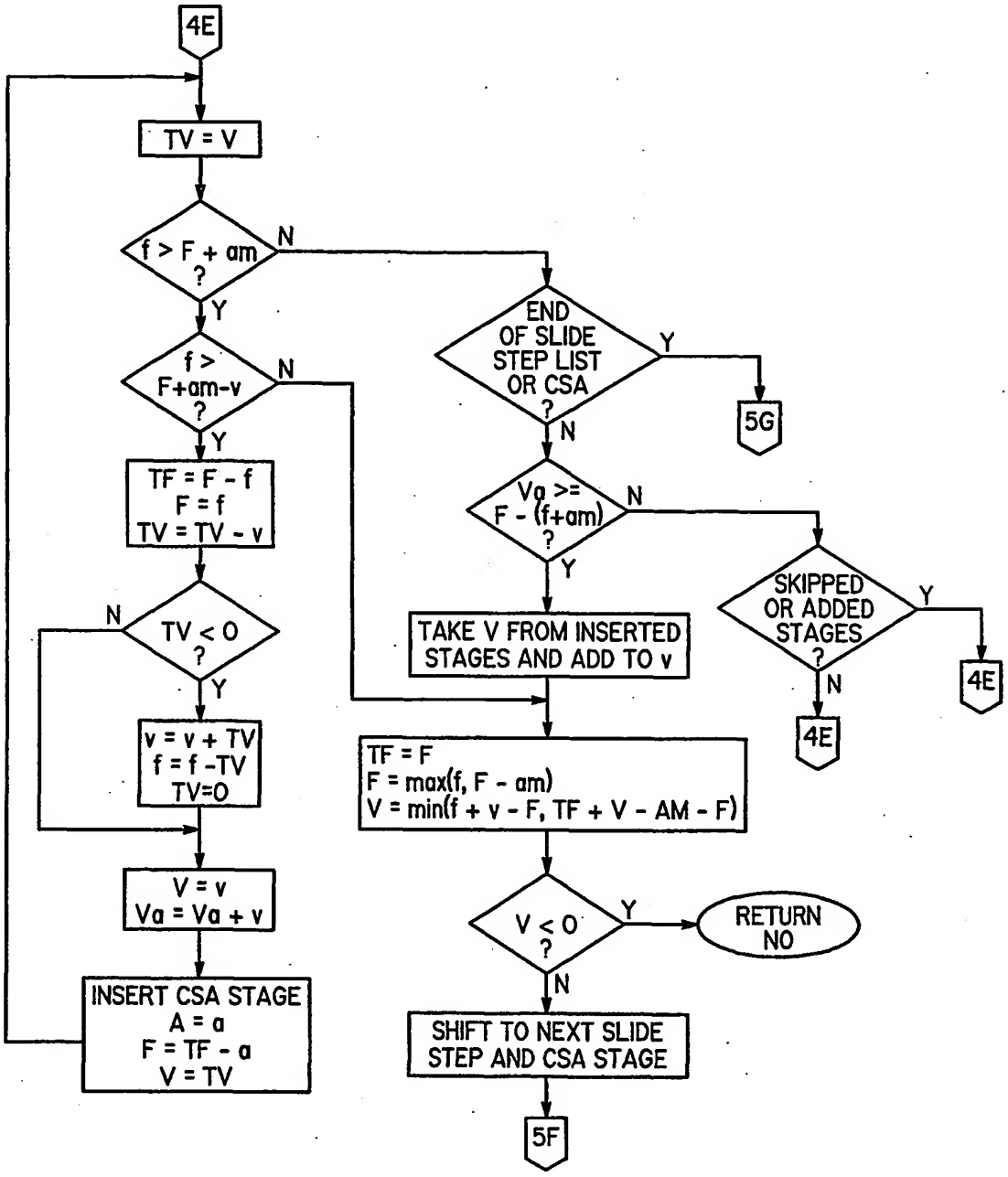
4E
TV = V
f > F + am ?
N
Y
f > F+am-v ?
N
Y
TF = F - f
F = f
TV = TV - v
N
TV < 0 ?
Y
v = v + TV
f = f -TV
TV=0
V = v
Va = Va + v
INSERT CSA STAGE
A = a
F = TF - a
V = TV
END OF SLIDE STEP LIST OR CSA ?
Y
5G
N
Va >= F - (f+am) ?
N
Y
SKIPPED OR ADDED STAGES ?
Y
4E
N
4E
TAKE V FROM INSERTED STAGES AND ADD TO v
TF = F
F = max(f, F - am)
V = min(f + v - F, TF + V - AM - F)
V < 0 ?
Y
RETURN NO
N
SHIFT TO NEXT SLIDE STEP AND CSA STAGE
5F

FIG. 9C

INTERNATIONAL SEARCH REPORT

Int[redacted]onal Application No
P[redacted]S 01/00512

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N1/31

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, PAJ, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 839 091 A (CORL MARK V ET AL) 17 November 1998 (1998-11-17)	23,27
A	column 3, line 43 -column 4, line 30; figures 1B,3	1-22, 24-26
A	US 5 919 553 A (KAVANAUGH CHRISTOPHER P) 6 July 1999 (1999-07-06) column 3, line 1 -column 3, line 30; figure 3	1-27
A	DE 197 36 470 A (SCHENCK ULRICH PROF DR MED) 4 March 1999 (1999-03-04) the whole document	1-27
A	US 5 573 727 A (KEEFE RAYMOND A) 12 November 1996 (1996-11-12) the whole document	1-27

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 May 2001	15/05/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Thomte, M

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
US 01/00512

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 92 01919 A (AUSTRALIAN BIOMEDICAL) 6 February 1992 (1992-02-06) the whole document	1-27

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 01/00512

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		JP 6504115 T	12-05-1994
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